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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/569,677	MANTYLA ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/27/06; 03/08/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Claims 1-21 are pending in this application for examination and are now under consideration.

Priority

Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e). This application is 371 PCT/IS04/00011 filed on 08/27/2004 and claims the priority date of Provisional application 60/497,935 filed on 08/27/2003. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). This application also claims the priority date of Spain application 6929 filed on 08/27/2003.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 03/08/2007 and 02/27/2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, examiner has considered and initialed the information disclosure statements.

Objections to Abstract

The Abstract of the disclosure is objected to because, Abstract should be on a separate sheet of paper. Correction is required. See MPEP § 608.01(b).

Objections to Specification

The use of the trademarks in the specification, for example, claim 13, has been noted in this application. The following trademarks appear: Aviclel™. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Appropriate correction is required.

Claim Objections

Claims 1 and 2 are objected, due to the following informality: The following claims contain abbreviations; Claims 1 and 2 have CBM in their claims. Examiner suggests at least in the first recitation of the abbreviations, expanding them to recite the full forms of what the abbreviation stands for. Appropriate correction is required.

Double Patenting rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of reference patent U.S. Patent No. 7,462,701 B2, date of patent 19/09/08. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an

examined application claims are not patentably distinct from the reference claims, because the examined claims are either anticipated by, or would have been obvious over reference claims. See, e.g., *In re Berg*, 140 F.3d 1428,46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir.1993); *In re Longi* 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-21 of the instant application are directed to a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising heterologous protein fused to a CBM intercepted by a proteolytic cleavage site, contacting said fusion protein with a functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest... said CBM protease is from the group of proteases consisting of enterokinase (EK)....comprising a EK catalytic (EKc) domain, said EKc encoded by a nucleic acid sequence of SEQ ID NO: 2 and said CBMs are CBM encoded by a region of the xylanase 10A gene from *Thermotoga maritima* and encoded by a sequence of SQ ID NO: 1...

Claims 1-22 of reference patent U.S. Patent No. 7,396,670 B2 are directed to a method of production and purification a soluble from a transgenic heterologous protein of interest from a transgenic plant...., comprising providing a fusion protein comprising heterologous protein fused to a CBM intercepted by a proteolytic cleavage site, contacting said fusion protein with a functional protease fuse to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the

heterologous protein of interest… said CBM protease is from the group of proteases consisting of enterokinase (EK).....comprising a EK catalytic (EKc) domain, said EKc encoded by a nucleic acid sequence of SEQ ID NO: 2 and said CBMs are CBM encoded by a region of the xylanase 10A gene from *Thermotoga maritima* and encoded by a sequence of SQ ID NO: 1. Furthermore, the preferred embodiments in the instant application and the allowed patent U.S. Patent No. 7,396,670 B2 are one and the same. The reference patent claims 1-22 therefore encompass a genus of polypeptides and encoding polynucleotides used in the process for purification of a heterologous protein of interest, which overlaps with the genus of genus of polypeptides and encoding polynucleotides used in the process for purification of a heterologous protein of interest of instant claims.

The claims 1-21 of the instant application cannot be considered patentably distinct over claims 1-22 of reference patent U.S. Patent No. 7,396,670 B2, when there is specifically recited embodiment in the reference patent which supports the claimed method i.e., a method of production and purification a soluble from a transgenic heterologous protein of interest from a transgenic plant...., comprising providing a fusion protein comprising heterologous protein fused to a CBM intercepted by a proteolytic cleavage site, contacting said fusion protein with a functional protease fuse to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest… said CBM protease is from the group of proteases consisting of enterokinase (EK).....comprising a EK catalytic (EKc) domain, said EKc encoded by a nucleic acid sequence of SEQ ID NO: 2 and said CBMs are

CBM encoded by a region of the xylanase 10A gene from *Thermotoga maritima* and encoded by a sequence of SQ ID NO: 1, that would anticipate claims 1-21 of the instant application. Alternatively, claims 1-21 of the instant application cannot be considered patentably distinct over claims 1-22 of reference patent U.S. Patent No. 7,396,670 B2 when there is specifically disclosed embodiment in the reference patent U.S. Patent No. 7,396,670 B2 that supports claims 1-22 of that patent and falls within the scope of the claims 1-21 herein, i. e., a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising heterologous protein fused to a CBM intercepted by a proteolytic cleavage site, contacting said fusion protein with a functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest... said CBM protease is from the group of proteases consisting of enterokinase (EK)....comprising a EK catalytic (EKc) domain, said EKc encoded by a nucleic acid sequence of SEQ ID NO: 2 and said CBMs are CBM encoded by a region of the xylanase 10A gene from *Thermotoga maritima* and encoded by a sequence of SQ ID NO: 1..., because it would have been obvious to one having ordinary skill in the art to modify claims 1-22 of reference patent U.S. Patent No. 7,396,670 B2 by selecting a specifically disclosed embodiment that supports those claims of the reference patent. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being preferred embodiment within claims 1-22 of reference patent U.S. Patent No. 7,396,670 B2.

Claim Rejections: 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-21 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 part (g) recites the phrase "... substantially to insoluble cell-wall plant material", there is insufficient antecedent basis for this limitation in the claim. Clarification and correction required.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 21 is rejected for the phrase "substantial sequence identity", as the metes and bounds are not clear. It is not clear to the examiner as to what percentage of identity is encompassed, as there is no numerical value and therefore the scope of the phrase "substantially equal to" is not clear to the examiner. Clarification and correction is required.

Claim Rejections: 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-4 and 6-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising heterologous protein fused to a CBM of SEQ ID NO: 1, a xylanase 10A gene from *Thermotoga*

maritima intercepted by a proteolytic cleavage site, contacting said fusion protein with a functional protease fused to a CBM, said functional protease is a bovine enterokinase catalytic domain of SEQ ID NO: 2, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest..., the specification does not reasonably provide enablement for a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM sequence having any undefined sequence identity to the amino acid sequence of SEQ ID NO: 1 (also see 112, second paragraph rejection) or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-4 and 6-21, recite a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM sequence having any undefined sequence identity to the amino acid sequence of SEQ ID NO: 1 (also see 112, second paragraph rejection) or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides or polynucleotides and encoded polypeptides from any source i.e., a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM sequence having any undefined sequence identity to the amino acid sequence of SEQ ID NO: 1 (also see 112, second paragraph rejection) or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease

fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest, broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein structure relates to its function.

In this case the disclosure is limited to a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising heterologous protein fused to a CBM of SEQ ID NO: 1, a xylanase 10A gene from *Thermotoga maritima* intercepted by a proteolytic cleavage site, contacting said fusion protein with a functional protease fused to a CBM, said functional protease is a bovine enterokinase catalytic domain of SEQ ID NO: 2, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest. In view of the broad breadth of the claims, the amount of experimentation required to determine the structure of all the polypeptides or polynucleotides and encoded polypeptides from any source in the recited method, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340), practicing the

claimed invention would require undue experimentation. As such, the specification fails to enable the entire scope of the claimed invention.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, it is not routine in the art to screen for any number of nucleic acids and encoding polypeptides or for multiple substitutions or multiple modifications as encompassed by the instant claims in view of the fact that the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish even further with each additional modification, e.g. multiple substitutions or deletions.

The specification does not support the broad scope of the claims because the specification does not establish: **(A)** the structure of all the polynucleotides and encoded polypeptides with the desired activity i.e., any CBM from any source including variants, mutants and recombinants or any CBM sequence having any undefined sequence identity to the amino acid sequence of SEQ ID NO: 1 or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants and any functional protease fused to a CBM; **(B)** regions of the protein/polynucleotide structure which may be modified without affecting the activity of said polypeptides; **(C)** the general tolerance of the polynucleotide and the encoding polypeptide to modification and extent of such tolerance; **(D)** a rational

and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; and **(E)** sufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides and encoding polypeptides with an enormous number of modifications and enormous number of wild-type strains from any source. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising heterologous protein fused to a CBM of SEQ ID NO: 1, a xylanase 10A gene from *Thermotoga maritima* intercepted by a proteolytic cleavage site, contacting said fusion protein with a functional protease fused to a CBM, said functional protease is a bovine enterokinase catalytic domain of SEQ ID NO: 2, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest, is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-4 and 6-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4 and 6-21 are directed to encompass a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM sequence having any undefined sequence identity to the amino acid sequence of SEQ ID NO: 1 (also see 112, second paragraph rejection) or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case the scope of the instant claims encompass a genus of structures for encoding polypeptides or polynucleotides and encoded polypeptides of interest, i.e., a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM sequence having any undefined sequence identity to the amino acid sequence of SEQ ID NO: 1 (also see 112, second paragraph rejection) or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest.

No information, beyond the characterization of an isolated Enterokinase catalytic domain comprising the amino acid sequence of SEQ ID NO: 2 and a CBM encoded by a polynucleotide sequence of SEQ ID NO: 1 has been provided by the applicants, which would indicate that they had possession of the claimed genus of structures for encoding polypeptides or polynucleotides and encoded polypeptides of interest, i.e., a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM sequence having any undefined sequence identity to the amino acid sequence of SEQ ID NO: 1 (also see 112, second paragraph rejection) or any CBM encoded by any region of the xylanase 10A gene from

Thermotoga maritima of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest.

The art also teaches, even highly structurally homologous polypeptides do not necessarily share the same function and conversely functionally similar molecules do not necessarily have similar structures. For example proteins having similar structure have different activities; Witkowski et al., (Biochemistry 38:11643-11650, 1999) teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Similarly, Wishart et al., (J. Biol. Chem., 1995, Vol. 270(10): 26782-26785) teach that a single mutation converts a novel phosphotyrosine binding domain into a dual-specificity phosphatase. The art also teaches that functionally similar molecules have different structures; Kisselev L., (Structure, 2002, Vol. 10: 8-9) teach that polypeptide release factors in prokaryotes and eukaryotes have same function but different structures.

Hence, the recited genera of polypeptides or polynucleotides and encoded polypeptides are interpreted to have widely variable structures, since minor changes may result in changes affecting function and no additional information correlating structure with function has been provided.

Therefore, given the lack of description of representative species encompassed by the genus of polypeptides or polynucleotides and encoded polypeptides and

modifications, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention. Applicants are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 6-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haynes et al., (US Patent No.: 6,048,715 in IDS) in view Shani et al., (WO 00/77174 A1 in IDS). Claims 1-4 and 6-20 are directed to a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease fused to a CBM, at conditions facilitating

proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest.

Haynes et al., disclose an aqueous phase separation system and/or purification systems, together with methods for their preparation and use, are provided which are based on polymer-ligand conjugates wherein the polymer and the composition to be separated and/or purified comprises a ligand which binds to the oligosaccharide polymer, the ligand is a polysaccharide binding peptide such as CBM which is an amino acid sequence characterized as capable of binding to a phase-forming oligosaccharide polymer, following binding the composition may be removed from the oligosaccharide polymer or by utilizing a specific or non-specific protease that can be used for enzymatic removal of the compound from the polysaccharide binding moiety which remains bound to the oligosaccharide polymer by incorporating a protease recognition sequence between the compound and the polysaccharide binding moiety (column 3, Summary of invention; column 19, Table 6: Cellulose binding domains; column 23; column 29, Example 1; column 31, Example 6; claims columns 51-54 and entire document).

The reference of Haynes et al., although discloses an aqueous phase separation system and/or purification systems, together with methods for their preparation and use (same as the instant invention), said reference is silent regarding said fusion proteins are expressed in transgenic plants or obtained from transgenic plants (as in claims 6-20).

Shani et al., disclose a process of expressing a recombinant protein in a plant and for isolating the recombinant protein from the plant, the process is effected by (a)

providing a plant, a plant derived tissue or cultured cells expressing a fusion protein including the recombinant protein and a cellulose binding peptide being fused therein, the fusion protein being compartmentalized within cells of the plant, plant derived tissue or cultured plant cells; (b) homogenizing the plant, plant derived tissue or cultured plant cells, so as to bring into contact the fusion protein with a cellulosic matter of plant, plant derived tissue or cultured plant cells, to thereby effect affinity binding of the fusion protein via the cellulose binding peptide to the cellulosic matter, thereby obtaining a fusion protein cellulosic matter complex; and (c) isolating the fusion protein cellulosic matter complex; said reference also teaches including insertion of a protease cleavage sites in the fusion protein for releasing the heterologous protein of interest from the CBD in the fusion protein (pages 14-16).

Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Haynes et al., and Shani et al., to develop a process for purification of a heterologous protein of interest, comprising providing a fusion protein comprising a heterologous protein fused to any CBM from any source including variants, mutants and recombinants or any CBM encoded by any region of the xylanase 10A gene from *Thermotoga maritima* of undefined structure including variants, mutants and recombinants, said fusion protein intercepted by a proteolytic cleavage site, contacting said fusion protein with any functional protease fused to a CBM, at conditions facilitating proteolytic cleavage by said protease, to cleave the CBM from the heterologous protein of interest. Motivation to do so derived from the combined teachings of Haynes et at., and Shani et al., that teach: (i) the advantages of fusion

proteins comprising CBD binding domain and proteolytic cleavage site for ease of isolation of heterologous protein of interest and (ii) plants represent an alternative expression system for mass production of many proteins of commercial interest (Shani et al., pages 3-4). The expectation of success is high, because Haynes et al., disclose an aqueous phase separation system and/or purification systems, together with methods for their preparation and use (same as the instant invention) and Shani et al., disclose a process of expressing a recombinant protein in a plant and for isolating the recombinant protein from the plant including recombinant fusion proteins comprising CBD and proteolytic cleavage sites.

Therefore, claims 1-4 and 6-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haynes et al., (US Patent No.: 6,048,715 in IDS) in view Shani et al., (WO 00/77174 A1 in IDS).

Allowable Subject Matter/Conclusion

None of the claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of

a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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